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4. BIOPHYSICS:
MEASUREMENT OF THE CRAWLING FORCE GENERATED BY AMOEBOID CELLS

The term "amoeba" (ameba) refers to a genus of single-celled protozoa characterized by the ability to continuously change shape by localized extension (pseudopod formation) and retraction, with shape-change used for both locomotion and engulfment of food. In contrast, the term "amoeboid movement" ("amoeboid cells"; "amoeba-like movement") refers to the movements of any cell of any genus, where the movement is effected by means of pseudopods and the shape of the cell is subject to constant change.

The organism Dictyostelium discoideum is a special case of a simple organism occurring in two basic forms: free individual cells and the same cells in an organized colony. Although often called a "cellular slime mold", D. discoideum is not a mold, nor is it consistently slimy. The term "social amoeba" is more accurate. When the organism is individualized, the entities are called "myxamoebae". When they aggregate into a slug, the organism is called a "pseudoplasmodium" or termed the "grex". The aggregation into a unitary grex may involve tens of thousands of individual amoebae. Experiments have demonstrated that the directional locomotion of myxamoebae is dependent on ambient gradients of cyclic adenosine-3',5'-monophosphate (cAMP).

"Motor proteins" are mechanico-chemical enzymes involved in locomotion of cells or transport of materials in cells, and there are three families of such proteins: kinesins, dyneins, and myosins. Kinesins and dyneins are microtubule-based motor proteins, while myosin is a microfilament-based motor protein. The microtubules are hollow cylinders approximately 24 nanometers in diameter, many microns in length, and consist of heterodimers of alpha- and beta-tubulin proteins plus a variable set of other proteins. Microfilaments are 4 to 6 nanometers in diameter, highly variable in length, and are found in all cells with internal membrane-bound organelles (eukaryotic cells). In general, as mechanico-chemical enzymes, motor proteins convert energy from hydrolysis of nucleotides to mechanical force, and since they are involved in many important cellular events, the molecular details are currently the focus of intensive research.

... ... **Y. Fukui et al (4 authors at 3 installations, US JP) present an analysis of the crawling force generated by cells undergoing amoeboid locomotion, the authors making the following points:**

1) Generation of mechanical forces is essential for cell locomotion, cell division, embryonic development, and morphogenesis. Although the forces involved in some of these biological activities have been measured as mechanical properties in local regions of living cells, few measurements have been made of the maximum ability of an entire cell to propel itself. An example is the measurement of the maximum propulsive force of 7 x 10^(3) piconewtons generated by a swimming ciliated protozoan, Paramecium caudatum, measured using a centrifuge microscope. In contrast, little is known of the propulsive forces that can be generated by any cell undergoing amoeboid movement.

2) The authors report measurement of the maximum "apparent weight" centrifugal force against which ordinary (wild-type) and myosin mutants of D. discoideum amoebae were able to crawl "upward". The small mass of the amoebae required the use of a recently developed centrifuge polarizing microscope capable of generating fields of greater than 11,465 g (where g = Earth's gravitational acceleration), with image resolution of better than 1 micron.

3) The authors report that D. discoideum mutant amoeba lacking myosin ("myosin knockout mutants") stall or cease to be able to crawl up against the imposed apparent weight at characteristic centrifugal accelerations, so they are least able to overcome that much external force. Those lacking the muscle type myosin (myosin II) stall at very much lower centrifugal acceleration.

4) The authors suggest that the mechanism of stalling, or inability of the amoeba to maintain directional locomotion against the centrifugal field, depends on the very high local density of its leading pseudopod rather than on the apparent weight felt by the whole amoeba. Even in media whose density is greater than that of the whole amoeba, amoebae lacking myosin II are unable to sustain the forward protrusion of the high-density pseudopod that is apparently needed for directional amoeboid locomotion against the external field.

5) The authors conclude: "We believe that the forward protrusion of the leading pseudopod is not simply a phenomenon observed in Dictyostelium and other amoebae, but that it is an essential feature for the directional migration of cells undergoing amoeboid locomotion in general. Once the direction of propagation is defined by some cue (e.g., cyclic adenosine-3',5'-monophosphate gradient for Dictyostelium amoebae) and a pseudopod starts forming in that direction, we suggest that the contractile force generated by the trailing cell cortex must provide adequate support for the pseudopod to penetrate into that direction without collapsing against the external force, whether

gravitational or a barrier presented (e.g., against leukocytes, parasitic *protista, or migrating embryonic cells) by a tissue layer... We postulate that the directional locomotion of an amoeboid cell requires the contractile cortical framework to provide the turgidity needed for the leading pseudopod to direct the locomotion in that direction."

Y. Fukui et al: How well can an amoeba climb?
(Proc. Natl. Acad. Sci. US 29 Aug 00 97:10020)
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Text Notes:
... ... *protista: (Protoctista; protists) The term "protista" refers to one of the phylogenetic kingdoms, this category defined mostly by exclusion and containing all the eukaryotic nucleated organisms that cannot be classified as animal, plant, or fungus. Protists include protozoans, algae, kelps, slime molds, and many obscure eukaryotes.

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